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The Role of Hypothalamic Corticotropin-Releasing Hormone on the High Salt Intake-Induced Active Coping Behaviors after the Innate Fear Stress in Mice.

Kenjiro Seki [1], Tohru Matsuki [2]

[1] Department of Pharmacology, School of Pharmaceutical Science, Ohu University,
[2] Department of Cellular Pathology, Institute for Developmental Research,
Aichi Developmental Disability Center

Summary

Background: We have previously reported that the 5 consecutive-days of 2% sodium salt intake which does not cause hypertension promotes the induction of active coping behavior during tail suspension test (TST) after the cessation of the inescapable innate fear for 5 min caused by a component of fox faces, 2,4,5-trimethylthiazoline (TMT). In addition, we found that the active coping behaviors during TST is significantly correlated with the preference of central zone during TMT-induced fear stress. This amount of sodium salt intake suppresses the expression of the corticotropin-releasing factor (CRF) in the hypothalamus even when the fear stress is subjected. In this study, we investigated whether the high salt intake affect to the anxiety level and tested whether the alteration of the anxiety level and then the overexpression of hypothalamic CRF prevent the high salt intake produces the correlation between central preference during TMT box and the active coping behavior during TST.

Methods: C57BL6/J mice (7-10 weeks old) with 2% salt or water-intake for 5 days were employed to the elevated plus maze (EPM) for 10 min 1 hour prior to the 10 min of TST. The immobility time as a coping behavior during TST for 10 min were recorded 1 hour after the TMT-induced fear stress in the acryl box (30×30×30 cm) in hypothalamic CRF overexpression (Hy-AAV-CRF) mice which were bilaterally injections of 0.1 μL adeno-associated virus vector (pAAV-PHP.eB) producing the CRF-AAV.

Results and Discussion: Two percent of salt-intake increased the number of entries and the time spent in the open arm of the EPM, indicating that high salt intake had an anxiolytic effect. However, neither the number of entries nor the time spent in the open arm of the EPM were correlated with immobility time during TST in sodium-intake mice. In Hy-AAV-CRF mice, the number of entries into the central area and the time spent in the central area during TMT-induced innate fear stress were similar to those in water-intake Hy-AAV-CRF mice, indicating that the effect of salt intake was abolished when CRF was overexpressed in the hypothalamus. Furthermore, the correlation between the preference of central zone in the box during TMT fear stress and immobility time during TST was disappeared in Hy-AAV-CRF mice. These results suggest that suppression of hypothalamic CRF expression by salt intake produces a central preference which is not produced by the lower anxiety level and the high salt-intake suppressed hypothalamic CRF expression is important for inducing the active coping behavior during TST.